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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|----------------------|------------------|
| 09/578,363 | 05/25/2000 | Barbara P. Wallner | 10248/7012 (ERG/MAT) | 6092 |

7590

05/07/2002

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EXAMINER

RUSSEL, JEFFREY E

ART UNIT

PAPER NUMBER

1653

DATE MAILED: 05/07/2002

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/578,363

Applicant(s)

WALLNER ET AL.

Examiner

Jeffrey E. Russel

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on March 4, 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8, 11-19, 31, 36 and 37 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 4-7, 11-19, 31, 36 and 37 is/are rejected.
- 7) ☒ Claim(s) 3 and 8 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 11-19, 31, 36, and 37 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 of copending Application No. 09/744,658 in view of O'Reilly et al or Brooks et al. Although the conflicting claims are not identical, they are not patentably distinct from each other. The '658 application claims treating medical conditions including angiogenesis, neoplasm, tumors, and cancer by administering a DPP-IV inhibitor, preferably Val-boroPro. See claims 10, 13, and 20. The '658 application does not claim combining its DPP-IV inhibitors with antiangiogenic or anti-cancer compounds, does not claim combining its DPP-IV inhibitor administration with surgical treatment, and does not claim the subjects being treated for angiogenesis, neoplasm, tumors, or cancer as being otherwise free of symptoms calling for hemopoietic stimulation, as having normal hemopoietic activity, or as being HIV negative. O'Reilly et al (see, e.g., column 14, lines 20-27) and Brooks et al (see, e.g., column 8, lines 13-25) disclose that it is known to combine surgical, chemotherapeutical, and anti-angiogenic treatments in treating tumors. It would have been obvious to one of ordinary skill to combine the angiogenesis, neoplasm, tumor and cancer treatment claimed in the '658 application with other known methods of treating

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angiogenesis, neoplasm, tumors, and cancer, including surgery or treatment with other anti-tumor compounds including angiogenesis inhibitors, because O'Reilly et al and Brooks et al show that it is routine in the cancer therapy arts to combine treatments in order to optimize treatment of the cancer. It would have been obvious to one of ordinary skill in the art to treat angiogenesis, neoplasm, tumors, and cancer according to the claimed method of the '658 application in any subject, including those patients recited in instant claims 11, 16, and 17, because it is desirable to treat angiogenesis, neoplasm, tumors, and cancer in any patient in which the conditions are found, and because the hemopoietic activity or HIV status of such a patient would not have been expected adversely to affect the patient's ability to be treated in the claimed method of the '658 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

2. Claims 1, 2, 11-19, 31, 36, and 37 are directed to an invention not patentably distinct from claims 1-21 of commonly assigned 09/744,658. See the above provisional obviousness-type double patenting rejection.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302).

Commonly assigned 09/744,658, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 37 CFR 1.78(c) and 35 U.S.C. 132 to either show that the conflicting

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inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

3. Instant claims 1-8, 11-17, 19, 31, 36, and 37 are not deemed to be entitled under 35 U.S.C. 119(e) to the benefit of the filing date of provisional application 60/135,861 because the provisional application, under the test of 35 U.S.C. 112, first paragraph, does not disclose the compounds of Formula II in which A and A₁ can be any L- or D-amino acid. Note that the provisional application at page 2 and page 11 requires the amino acid attached to the N-terminus of A₁ to be a proline residue, which is not required by Formula II as recited in the instant claims. Note also that page 2, line 24, and page 11, line 22, of the provisional application explicitly require the amino acids present in the compounds of Formula II to be L-amino acids. Accordingly, the WO Patent Application 00/10549 is now available as prior art against these claims under 35 U.S.C. 102(a).

Instant claim 18 is deemed to be entitled under 35 U.S.C. 119(e) to the benefit of the filing date of provisional application 60/135,861 because the provisional application, under the test of 35 U.S.C. 112, first paragraph, is deemed to disclose the claimed invention.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

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4. Claims 1, 2, 11-17, 19, 31, 36, and 37 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 00/10549 in view of O'Reilly et al or Brooks et al. The WO Patent Application '549 teaches treating medical conditions including angiogenesis, neoplasm, tumors, and cancer by administering a DPP-IV inhibitor, preferably Val-boroPro. The DPP-IV inhibitors can be administered in combination with other therapeutic agents, or can be combined with more traditional therapies. See, e.g., the Abstract; page 4, lines 25-32; page 5, lines 9-12; page 13, lines 23-27; and claim 13. The WO Patent Application '549 does not specifically teach combining its DPP-IV inhibitors with antiangiogenic or anti-cancer compounds, does not specifically teach combining its DPP-IV inhibitor administration with surgical treatment, and does not describe the subjects being treated for angiogenesis, neoplasm, tumors, and cancer as being otherwise free of symptoms calling for hemopoietic stimulation, as having normal hemopoietic activity, or as being HIV negative. O'Reilly et al (see, e.g., column 14, lines 20-27) and Brooks et al (see, e.g., column 8, lines 13-25) disclose that it is known to combine surgical, chemotherapeutical, and anti-angiogenic treatments in treating tumors. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to combine the tumor treatment of the WO Patent Application '549 with other known methods of treating angiogenesis, neoplasm, tumors, and cancer, including surgery or treatment with other anti-tumor compounds including angiogenesis inhibitors, because O'Reilly et al and Brooks et al show that it is routine in the cancer therapy arts to combine treatments in order to optimize treatment of the cancer, and because the WO Patent Application '549 discloses the desirability of combining treatment using DPP-IV inhibitors with treatment using other therapeutic agents or with more traditional therapies. It would have been obvious to one of

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ordinary skill in the art at the time Applicants' invention was made to treat angiogenesis, neoplasm, tumors, and cancer according to the method of the WO Patent Application '549 in any subject, including those patients recited in instant claims 11, 16, and 17, because it is desirable to treat angiogenesis, neoplasm, tumors, and cancer in any patient in which the conditions are found, and because the hemopoietic activity or HIV status of such a patient would not have been expected adversely to affect the patient's ability to be treated in the method of the WO Patent Application '549, and because the WO Patent Application '549 does not set forth any limitations on the type of subjects who can be treated for angiogenesis, neoplasm, tumors, and cancer.

5. Claims 1, 2, 4-7, 11-17, 31, 36, and 37 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 95/15309 in view of O'Reilly et al or Brooks et al. The WO Patent Application '309 teaches preventing the metastases of breast and prostate tumors to the lungs by administering DP-IV inhibitors. DP-IV inhibitors include compound numbers 41-45 at pages 17-18, which have a boronate ester group which is labile in water giving the free boronic acid esters, and which therefore meet the requirements of Applicants' Formula II. See, e.g., the abstract; page 3, lines 10-11 and 17-18; and page 6, lines 11-14. Breast and prostate tumors are epithelial in origin. The WO Patent Application '309 does not describe the subjects being treated for tumors as being otherwise free of symptoms calling for hemopoietic stimulation, as having normal hemopoietic activity, or as being HIV negative. However, the WO Patent Application '309 does not set forth any limitations on the type of subjects who can be treated for breast and prostate tumors and to prevent metastases. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to treat breast and prostate tumors and to prevent metastases according to the method of the WO Patent Application

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'309 in any subject, including those patients recited in instant claims 11, 16, and 17, because it is desirable to treat breast and prostate tumors and to prevent metastases in any patient in which tumors are found, and because the hemopoietic activity or HIV status of such a patient would not have been expected adversely to affect the patient's ability to be treated in the method of the WO Patent Application '309. The WO Patent Application '309 does not disclose combining their inhibitors with other anti-cancer or anti-angiogenic compounds in the treatment of tumors, and do not disclose practicing their method in combination with surgical methods of tumor treatment. O'Reilly et al (see, e.g., column 14, lines 20-27) and Brooks et al (see, e.g., column 8, lines 13-25) disclose that it is known to combine surgical, chemotherapeutical, and anti-angiogenic treatments in treating tumors. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to combine the tumor treatment of the WO Patent Application '309 with other known methods of treating tumors, including surgery or treatment with other anti-tumor compounds including angiogenesis inhibitors, because O'Reilly et al and Brooks et al show that it is routine in the cancer therapy arts to combine treatments in order to optimize treatment of the cancer.

6. Claim 19 is rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 95/15309 in view of O'Reilly et al or Brooks et al as applied against claims 1, 2, 4-7, 11-17, 31, 36, and 37 above, and further in view of the WO Patent Application 00/10549. The WO Patent Application '309 does not teach or suggest that its DP-IV inhibitors inhibit angiogenesis. The WO Patent Application '549 teaches that DPP-IV inhibitors are useful for treating angiogenesis. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made in the method of the WO Patent Application '309 as modified

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above by O'Reilly et al or Brooks et al that angiogenesis would also be inhibited because the WO Patent Application '549 teaches that DP-IV inhibitors are useful for treating angiogenesis.

7. Applicant's arguments filed March 4, 2002 have been fully considered but they are not persuasive.

Copending application 09/744,658 is not provisionally available as prior art under 35 U.S.C. 102(e) against the instant application because the instant application was filed prior to November 29, 2000 and has not been voluntarily published under 35 U.S.C. 122(b), and because the '658 application did not meet the requirements of 35 U.S.C. 371(c)(1)(2) and (4) until May 30, 2001. See MPEP 1895.01(E)(1), first paragraph, and MPEP 2136.03(III), second paragraph.

The rejections based upon the WO Patent Application 95/15309 as the primary reference are maintained. The WO Patent Application '309 does teach DP-IV inhibitors including compound numbers 41-45 at pages 17-18, which have a boronate ester group which is labile in water giving the free boronic acid esters, and which therefore meet the requirements of Applicants' Formula II. The A substituents of compounds 41-45 are amino acids corresponding to Applicants' A₁ in Formula II. Applicants' claims do not require the amino acids to be present in Formula II to be naturally-occurring amino acids; otherwise, A and A₁ could not be D-amino acids as is explicitly recited in the claims. Concerning O'Reilly et al and Brooks et al, it is sufficient that these references suggest the combination of only one anti-angiogenic compound with surgery or chemotherapy in order to support the obviousness rejection set forth above. Applicants' claims which require the combination including an anti-angiogenic compound do not require that all anti-angiogenic compounds be used; they only require the use of one. Further, O'Reilly et al and Brooks et al suggest combining chemotherapy with surgery generally, and this

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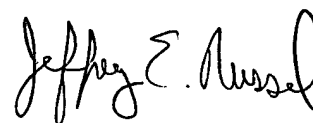
supports the obviousness of Applicants' claims aside from the issue of the combined use of anti-angiogenic agents.

The rejections set forth in the previous Office action based upon Zimmerman et al (U.S. Patent No. 5,767,242) in view of Bachovchin (U.S. Patent No. 5,965,532) are withdrawn, especially for the reasons given in Applicants' response at page 12, second full paragraph.

8. Claims 3 and 8 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The prior art of record does not teach or suggest treating a condition characterized by reactive stromal fibroblasts, or treating bone or connective tissue sarcomas, using a compound having the structure recited in instant claim 1.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Christopher Low can be reached at (703) 308-2923. The fax number for Art Unit 1653 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 305-7401 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.



Jeffrey E. Russel
Primary Patent Examiner
Art Unit 1653

JRussel
May 3, 2002